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Serum vitamin d levels in children with vitiligo

Vitamin D levels in pediatric vitiligo

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Abstract

Aim: In this study, we aimed to investigate the clinical profile of pediatric vitiligo in Turkey by analyzing differences in gender, clinical features, triggering factors, age of onset, duration of disease, atopy, familial history, and sun exposure in order to report the serum vitamin D levels of children with vitiligo. Material and Method: During a six-month period, 39 children with vitiligo and 39 healthy controls were studied. Demographic details were noted, and dermatological examination was performed to note the areas involved, leukotrichia, and halo nevus. 25-OH vitamin D was carried out by chemiluminescent enzyme immunoassay. Results: The group of girls with vitiligo was compared for serum 25-OH vitamin D levels. Significant differences were found between the girls in the control group, even if there were no significant differences between the group of boys with vitiligo and the control group. There were statistically significant differences in 25-OH vitamin D levels between the groups of girls and boys with vitiligo. Only 12 children had a history of more than 15 minutes of sunshine exposure per day, and a significant difference was noted among the boys. Vitamin D deficiency and insufficiency was found in 20 (5%) and 46 (1%) of children, respectively. Discussion: The antioxidant properties of vitamin D show protection from vitiligo. The low levels of vitamin D in girls with vitiligo are caused by concealing clothing, no daily supplementation of vitamin D, exposure to sunlight, more indoor work, and dark skin. These factors may contribute to the pathogenesis of vitiligo.

Keywords

Children; Vitamin D; Vitiligo

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Introduction

Vitiligo is a pigmentary disorder caused by autoimmune destruction of melanocytes [1]. Vitiligo affects about 0.5-2% of people worldwide, with half of the cases of vitiligo beginning under the age of 18, mostly in females [2]. The pathogenesis of vitiligo includes the unification of genetic propensity paired with environmental triggers such as stress, sun exposure, koebnerization and oxidative stress [3].

Vitamin D is a fat-soluble prohormone steroid that ensures the integrity of epidermal melanin units by controlling the activation, proliferation, and migration of melanocytes and pigmentation pathways as a result of modulating T-cell activation, which is apparently correlated with melanocyte disappearance in vitiligo [4]. Although it is known that the protective mechanism of vitiliginous skin is caused by an antioxidant activity of vitamin D and regulatory function against the reactive oxygen species, the full relationship between vitamin D and vitiligo is not yet fully understood.

In the literature, there are a few studies that analyze the clinico-epidemiologic profile of pediatric vitiligo through the clinical features of different ages of onset and the relationship of pediatric vitiligo to other autoimmune diseases.

This study aims to establish the profile of pediatric vitiligo in the southeastern region of Turkey by analyzing differences in gender, clinical features, triggering factors, age of onset, duration of disease, atopy, family history, and sun exposure in order to report the serum vitamin D levels of children with vitiligo.

Material and Methods

In this prospective study, the data of 78 children up to 17 years old were collected from July 2016 to December in 2016 in Mehmet Akif Inan Research and Training Hospital in Sanliurfa, Turkey. Demographic details such as age, gender, family history, age of onset, duration of disease, atopy, autoimmune diseases, triggering factors, sun exposure, distribution of lesions, and medical history were noted for all 39 children with vitiligo. A complete dermatological examination was performed, and the areas involved, leukotrichia, and halo nevus were noted. 25-OH vitamin D was carried out by chemiluminescent enzyme immunoassay from blood samples that were collected in the morning.

In the study, vitamin D deficiency, insufficiency, and sufficiency were defined as serum 25-OH vitamin D levels of <15ng/ml, 15-30ng/ml, and >30ng/ml, respectively.

In this study, patients were divided into six groups according to the standard study classification of vitiligo as follows: focal, segmental, vulgaris (generalized), acrofacial, mucosal, and universal. The participants were excluded if they had any other autoimmune or chronic diseases (e.g. thyroid disease, Addison's disease, diabetes mellitus, pernicious anemia, alopecia areata) or had been using vitamin D supplements, NSAIDs, systemic steroids in the previous three months. The controls were 39 healthy gender- and age-matched children with no family history of vitiligo or systemic autoimmune diseases. They were enlisted on the same day as the patients to avoid seasonal effects.

This study was approved by the University of Harran ethical committee (Report number: 161215). All of the parents were informed about the study and written approvals were received from them.

Statistical Analysis

The Kolmogorov-Smirnov test was used to determine the distribution normality of each variable. The Students' T-test was used for the comparison of means between the two groups. The Chi-Square test was applied for the analysis of categorical variables. SPSS 22.00 for Windows was used for all the analyses. The results with p-values of < 0.05 were defined as significant.

Results

Of the 39 children with vitiligo who visited the dermatology outpatient department over a period of six months, their ages, genders, and Fitzpatrick skin types were similar to those of children with vitiligo and the controls. In the present study, 22 (56.4%) were boys and 17 (43.6%) were girls. The mean age of onset was 9.1 years old, ranging from 1-16. The mean age of children at the visit was 10.7, ranging from 1-17. The duration of the disease varied from less than one month to 96 months with a mean duration of 19 months. Three patients (7.6%) had an onset between the ages of 0-4, seven (17.9%) between 5-8 years, 12 (30.7%) between 9-12 years, and 17 (43.8%) after 12 years. There was no statistical difference between genders with respect to the mean age of onset ($p=0.216$) or duration of disease ($p=0.435$). The most common type of vitiligo in the present study was acrofacial (41.0%), followed by vitiligo vulgaris (30.8%), focal vitiligo (25.6%), and segmental vitiligo (2.6%). Mucosal and universal vitiligo were not seen in either gender. The difference was not significant when the frequencies of the different types of vitiligo were compared with gender ($p=0.260$).

The clinical characteristics, treatment history, and serum 25-OH levels of girls and boys are shown in Table 1. Eleven boys and one girl with vitiligo experienced exposure to natural sunlight for more than 15 minutes per day, and there was a statistical difference between genders ($p=0.002$). Emotional stress was a triggering factor of vitiligo in 12 girls and four boys. There was a statistical difference between genders ($p=0.001$).

When 25-OH vitamin D levels were evaluated, vitamin D deficiency and insufficiency was found in 20.5% and 46.1% of children, respectively.

The mean levels of 25-OH vitamin D in children with vitiligo were 26.8 ± 9.6 ng/ml, ranging from 8.14 ng/ml to 58.07 ng/ml. The control group's mean level was 28.5 ± 9.4 ng/ml. The serum 25-OH vitamin D levels were not significantly different between children with vitiligo and the controls, but there were statistically significant differences in 25-OH vitamin D levels between the group of girls and boys with vitiligo ($p< 0.001$) (Table 1). When the group of girls with vitiligo was compared for serum 25-OH vitamin D levels, significant differences were found between the control group of girls, even if there were no significant differences between the group of boys with vitiligo and the controls (Table 2).

Discussion

The pathogenesis of vitiligo is not clear, but a high frequency of cytotoxic T lymphocytes specific to melanocytic antigens in reactive oxygen species are produced in vitiligo lesions. Vitamin D plays a role in the protection of vitiliginous skin from reactive oxygen species. In addition, vitamin D reduces the apoptotic activity induced by UVB and provides protection for the melanin unit [4,5].

Table 1. Clinical characteristics of children with vitiligo

	Girls	Boys	P value
Number of	17 (%43,6)	22 (%56,4)	NS
Age	12,0(±3,5)	10,09(±4,5)	NS
Disease duration	2,0(±1,5)	1,5(±1,6)	NS
Familiy history	3	7	NS
Sunshine exposure (>15 min)	1	11	0,002
Atophy	11	8	NS
Associated autoimmune disorders	1	1	NS
Fitzpatrick skin type :			
Type 1	-	-	
Tyep 2	-	5	NS
Type 3	8	11	NS
Type 4	7	5	NS
Type 5	2	1	NS
Triggering factor of Vitiligo:			
Koebnerization	2	6	NS
Emotional stress	12	4	0,001
Sunburn	1	7	NS
No flare up	2	5	NS
Halo nevus	6	2	NS
Leucotrishia	3	1	NS
Previous treatment:			
No treatment	5	12	NS
Topical steroids	6	6	NS
Topical calcineurin inhb	5	3	NS
Uvb	2	-	NS
Treatment total	13	9	NS
25(OH) D vit levels	19,1 (±8,2)ng/ml	29,7 (±8,07)ng/ml	<0,001

Min: minutes; 25(OH)D vit: 25-hydroxy vitamin D; NS: non-significant (p > 0.05)

Table 2. 25(OH) D vitamin levels of the patients with vitiligo and controls

	Control	Patients	P value
Number of girls	15	17	NS
Number of boys	24	22	NS
25(OH) D vit levels of girls	28,5 ng/ml	19,1 (±8,2)ng/ml	0,017
25(OH) D vit levels of boys	28,6 ng/ml	29,7 (±8,07)ng/ml	NS

25(OH)D vit: 25-hydroxy vitamin D; NS: non-significant (p > 0.05)

Although there have been several studies about pediatric vitiligo in Korea, China, India, the United States, and Kuwait, only one study was done in Turkey in 2016 [1,4,6-13]. To our knowledge, this was the first study that separately compared serum vitamin D levels in girls and boys with vitiligo.

The prevalence of pediatric vitiligo in girls was reported in previous studies; in Korea and China, however, a practically equal incidence in girls and boys was noticed [10,14,15]. In Turkey, Topal et al. and Gonul et al. reported almost similar results in adults with vitiligo [6]. In contrast, we observed gender equality in children [10,14].

The mean age of onset was between the ages of 4-8 in the United States, Korea, and China [9, 10, 14, 15] except two studies in India which were between the ages 8 and 12 [12,13]. In our study, the mean age of onset was 9.1, and 43% of children with vitiligo had an onset between the ages of 8-12. In Korea, the reason was a lack of clear pathogenesis of vitiligo, but in Kuwait, it was a lack of awareness and illiteracy. This was also true in Turkey.

In previous studies in Turkey, India, and China, the average duration of the disease ranged from 13-27 months, but our result, 19 months, was consistent with the result of Hu et al. [7,12,14].

In pediatric vitiligo, a family history of vitiligo from 3.3% to 46% has been reported [6-13]. However, Topal et al. noted a family history in 27% of patients, which was similar to our findings [6]. Depending on the frequency of consanguineous marriages in Turkey and surrounding countries high rates could be observed. Acrofacial vitiligo was the most common clinical type of pediatric vitiligo which is in contrast to previous studies in which vitiligo vulgaris was the most commonly reported type in adults. Agarwal et al. found that acrofacial was the most common due to ethnic and genetic diversity, as in Turkey [12].

As a triggering factor of vitiligo, koebnerization was noted in 15% of the subjects in our study. The prevalence of koebnerization in pediatric vitiligo is not clear. However, other triggering factors such as emotional stress and sunburn were observed in 41% and 30.8% of subjects, respectively. The level of emotional stress was significantly higher in girls with vitiligo. This may be caused by proximity to the civil war in Syria and exposure to the psychological trauma of social pressure to get married at an early age.

Halder et al. reported only two cases of alopecia areata in 82 children, which was similar to our study [8]. As already known in previous studies, the frequency of autoimmune diseases in children with vitiligo is very low [11].

In the present study, serum vitamin D deficiency and insufficiency were noted in 20.5% and 46.1% of patients, respectively. Similar observations were reported in a study by Hatun et al., in Turkey [18]. When the group of girls with vitiligo was compared for serum 25-OH vitamin D levels, significant differences were found between them and the control group of girls. Therefore, vitamin D deficiency in vitiligo may be among the factors that cause it, as mentioned in previous studies. In addition, there were statistically significant differences in 25-OH vitamin D levels between the group of girls and the group of boys with vitiligo. This is thought to be related to the exposure of boys to more than 15 minutes of sunlight per day. In Turkey and the Middle-East, a few studies showed that important factors in vitamin D deficiency were concealing clothing, no supplementation of vitamin D in daily use, less exposure to sunlight, more indoor work, and dark skin [16-20].

In conclusion, pediatric vitiligo may differ between genders in children as well as in adults. This may be a result of many factors, though vitamin D has attracted attention recently. We suggest that antioxidant activity of vitamin D may be a protective mechanism of vitiligo in patients who have a higher risk for deficiency and insufficiency of vitamin D, have a history of less than 15 minutes of sunlight exposure per day, spend most of the daytime at home, or wear concealing clothing. This study showed that girls are at greater risk for these reasons. The clinician should keep in mind that serum vitamin D levels may be lower in girls with vitiligo, but studies of larger groups of various racial identities are needed to verify or confirm our findings.

Scientific Responsibility Statement
The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest
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